

**In the claims:**

Please cancel claims 3, 21 and 25 without prejudice to pursue the subject matter of these claims in another application.

Please amend claims 1, 4, 19, 22, 23, 26 and 32 as follows:

- 1. (CURRENTLY AMENDED) A method for treating a condition associated with the excess accumulation of extracellular matrix in a tissue and/or organ or at a dermal wound site comprising:
  - a) reducing the excess accumulation of extracellular matrix associated with  $TGF\beta$  overproduction and/or activity in an organ or tissue, or at a wound site, by administering in an amount sufficient to inhibit  $TGF\beta$  overproduction and/or activity, a first agent that reduces  $TGF\beta$ -associated accumulation of extracellular matrix; and
  - b) degrading excess accumulated extracellular matrix in said tissue and/or organ or wound site, by administering in an amount sufficient to degrade excess accumulated extracellular matrix, a different, second agent that degrades extracellular matrix,whereby the accumulation of extracellular matrix in said tissue and/or organ or wound site is reduced from the level existing at the time of treatment.
2. (ORIGINAL) The method of claim 1 wherein the accumulation of extracellular matrix is reduced to a level which does not interfere with normal functioning of the tissue or organ or result in scarring.
3. (CANCELLED)
4. (CURRENTLY AMENDED) The method of Claim ~~3~~ 1 wherein said first agent

that inhibits TGF $\beta$  reduces TGF $\beta$ -associated accumulation of extracellular matrix  
is selected from the group consisting of ~~selected from the group consisting of~~  
inhibitors of aldosterone, inhibitors of angiotensin II, anti-TGF $\beta$  antibodies, renin,  
ACE inhibitors, AII receptor antagonists, proteoglycans and ligands for the TGF $\beta$   
receptor.

5. (WITHDRAWN)
6. (ORIGINAL) The method of claim 4 wherein said ACE inhibitor is Enalapril<sup>tm</sup>.
- 7-8. (WITHDRAWN)
9. (ORIGINAL) The method of claim 1 wherein said step of degrading excess accumulated extracellular matrix comprises contacting said matrix with at least one protease in an amount sufficient to degrade excess accumulated extracellular matrix to a level that does not impair the normal function of said tissue and/or organ or result in scarring.
10. (ORIGINAL) The method of claim 9 wherein said protease is selected from the group consisting of serine proteases, metalloproteinases and protease combinations.
11. (ORIGINAL) The method of claim 1 wherein said step of degrading accumulated extracellular matrix comprises administering an agent which increases the amount of active protease sufficient to degrade excess accumulated matrix to a level that does not impair the normal function of said tissue and/or organ or result in scarring.

12. (ORIGINAL) The method of claim 11 wherein said protease is selected from the group consisting of serine proteases, metalloproteinases and protease combinations.
13. (ORIGINAL) The method of claim 12 wherein said protease is plasmin and said agent which increases the amount of active plasmin is tPA.
14. (WITHDRAWN)
15. (ORIGINAL) The method of claim 1 wherein said condition associated with the excess accumulation of extracellular matrix is a fibrotic condition.
16. (ORIGINAL) The method of claim 15 wherein said fibrotic condition is selected from the group consisting of glomerulonephritis, adult or acute respiratory distress syndrome (ARDS), diabetes, diabetic kidney disease, liver fibrosis, kidney fibrosis, lung fibrosis, post infarction cardiac fibrosis, fibrocystic diseases, fibrotic cancer, post myocardial infarction, left ventricular hypertrophy, pulmonary fibrosis, liver cirrhosis, veno-occlusive disease, post-spinal cord injury, post-retinal and glaucoma surgery, post-angioplasty restenosis, renal interstitial fibrosis, arteriovenous graft failure and scarring.
17. (ORIGINAL) The method of claim 1 wherein said tissue or organ is selected from the group consisting of kidney, lung, liver, heart, arteries, skin and the central nervous system.
18. (ORIGINAL) The method of claim 1 wherein said condition associated with the excess accumulation of extracellular matrix is scarring.

19. (CURRENTLY AMENDED) The method of claim ~~3~~ 1 wherein said first agent that ~~inhibits~~ TGF $\beta$  reduces TGF $\beta$ -associated accumulation of extracellular matrix is nucleic acid encoding the agent.
20. (ORIGINAL) The method of claim 9 wherein said protease is nucleic acid encoding a protease.
21. (CANCELLED)
22. (CURRENTLY AMENDED) The method of claim ~~21~~ 1, wherein said first agent that ~~inhibits~~ TGF $\beta$  reduces TGF $\beta$ -associated accumulation of extracellular matrix and said second agent ~~to degrade~~ that degrades excess accumulated extracellular matrix are administered concurrently.
23. (CURRENTLY AMENDED) The method of claim ~~21~~ 1 wherein said first agent that ~~inhibits~~ TGF $\beta$  reduces TGF $\beta$ -associated accumulation of extracellular matrix and said second agent ~~to degrade~~ that degrades excess accumulated extracellular matrix are administered sequentially.
24. (WITHDRAWN)
25. (CANCELLED)
26. (CURRENTLY AMENDED) A method for treating or preventing a condition associated with the excess accumulation of extracellular matrix in a tissue and/or organ, or at a wound site, comprising administering in an amount sufficient to inhibit TGF $\beta$  activity and/or production, a combination of at least one first agent and at least one second agent, ~~agents in an amount sufficient to inhibit TGF $\beta$  activity and/or production~~ to prevent or reduce the excess accumulation of

extracellular matrix associated with TGF $\beta$  overproduction in a tissue and/or organ, or at a wound site, said first agent an agent that reduces TGF $\beta$ -associated accumulation of extracellular matrix, and said second agent an agent that degrades extracellular matrix.

27-29. (WITHDRAWN)

30. (ORIGINAL) The method of claim 26 wherein said agents are nucleic acids encoding said respective agents.
31. (ORIGINAL) The method of claim 26 wherein said agents are administered to reduce TGF $\beta$  overproduction prior to excess accumulation of extracellular matrix.
32. (CURRENTLY AMENDED) A method for preventing or reducing excess extracellular matrix accumulation in a tissue or organ or at a wound site comprising inhibiting the overproduction of TGF $\beta$  present in an organ or tissue or at a wound site to prevent the excess accumulation of extracellular matrix by administering a combination of agents that inhibit TGF $\beta$  activity and/or production to a subject, in an amount sufficient to inhibit TGF $\beta$  activity and/or production, said agents comprising at least one first agent that reduces TGF $\beta$ -associated accumulation of extracellular matrix, and at least one, different, second agent that reduces TGF $\beta$ -associated accumulation of extracellular matrix, such that administration of a combination of the first and second agent results in greater reduction in accumulation of excess extracellular matrix than either agent does alone.
33. (ORIGINAL) The method of claim 32 further comprising the step of degrading excess accumulated extracellular matrix in said tissue and/or organ or at said wound site.

34. (ORIGINAL) The method of claim 32 wherein said accumulation of extracellular matrix is reduced to a level which does not interfere with the normal functioning of the tissue and/or organ in which said extracellular matrix accumulated or scarring is prevented or reduced.

35-54. (WITHDRAWN)

55. (PREVIOUSLY PRESENTED) The method of claim 52, further comprising the step of administering an agent or combination of agents that inhibit TGF $\beta$  activity and/or production.